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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,525	07/09/2001	Jay M. Short	DIVER1230-2	7453

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/902,525	SHORT ET AL.	
	Examin r	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *02 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-92* is/are pending in the application.

4a) Of the above claim(s) *24-39,42-66 and 86-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,40,41 and 67-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-92 are at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-23, 40, 41 and 67-85 and SEQ ID NOs: 21 and 30, drawn to an isolated nucleic acid molecule encoding a polypeptide having thermostable phosphatase activity, in Paper No. 10 is acknowledged. The traversal is on the ground(s) that search and examination of SEQ ID NOs: 22, 31, 23, 32, 26, 25, 45 and 46 as a part of Group I in addition to SEQ ID NOs 21 and 30, would not present an undue burden on the examiner because each of these additional polypeptides and the nucleic acids encoding them have similar modes of operation, similar functions and similar effects as all the polypeptides were derived from the *Thermococcus* species and all have phosphatase activity. This argument is not found persuasive because each of the additional nucleic acid and amino acid sequences are completely different structural molecules that while the search and examination of all of the sequences in question may overlap, they are not coextensive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 24-39, 42-66 and 86-92 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 9.

Priority

Applicants statement on the first line of the specification to state that this application is a continuation-in-part of U.S. Application Serial No. 09/202,681, filed December 23, 1999, now pending, which is a national stage Application of US97/10784, filed June3 19, 1997; which claims the priority to U.S. Provisional Application Serial No. 60/033,752, the contents of which are hereby incorporated by reference in their entirety is acknowledged.

Information Disclosure Statement

Applicants filing of information disclosure, Paper No. 10, filed 2/9/2000, is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities:

On page 7 of the specification in the "Brief Description of the Drawings", for Figure 5-13, applicants recite "...and corresponding deduded amino acid sequence...". It is believed that this should be amended to "...and corresponding deduced amino acid sequence...".

Page 73, the first page of the "Examples" does not have a page number.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth: Example 1 lists a number of primer

sequences that do not appear to have an associated sequence identifier (i.e. SEQ ID NO). Additionally these primers are presented such that the first primer of each set carries over to a second line, and then after a single space the second primer is listed. This presentation is unclear.

Further applicants have a number of Figures which contain amino acid or nucleic acid sequences. As per MPEP: **2422.02** The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures. It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings.

Appropriate correction is required.

Claim Objections

Claim 1-23, 40, 41 and 67-85 is objected to because of the following informalities:

Claim 1-23, 40, 41 and 67-85 each contain nonelected subject matter.

Claim 85 recites "A polynucleotide probe" in contrast to most of the other claims which recite "A nucleic acid probe". It is suggested that applicants maintain consistency throughout the application and thus either refer to a "polynucleotide probe" or a "nucleic acid probe" unless there is a reason for the use of the different terms.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3-5, 6-14, 15, 17-21, 67-81, 82, 83 and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite in that it is drawn to the nucleic acid of claim 1, comprising a sequence selected from the group consisting of SEQ ID NO: 21, sequences substantially identical thereto, and sequences complementary thereto. As applicants specification at page 12, lines 6 through line 13, defines those nucleic acid sequences that are "substantially identical thereto" as having at least 50% nucleotide sequence identity over a region of at least about 100 residues, claim 2 appears to be broader in scope then claim 1 which is drawn to a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NO: 21, and variants thereof having at least 50% identity to SEQ ID NO: 21. As claim 1 is interpreted as the 50% identity is based on the entire sequence of SEQ ID NO: 21, which is 765 bp long, claim 2 is broader in scope then claim 1.

Claims 3-5, 67-81, 82, 83 and 84 are indefinite in the recitation of the terms "high, moderate and low stringency" as the specification does not define what conditions constitute "stringent". While page 13 and 40 of the specification describe some conditions which are encompassed by various hybridization stringencies, there is

nothing to suggest that other conditions would not also be included within the scope of these terms and in the art what is considered high, moderate and low stringency varies widely depending on the individual situation as well as the person making the determination. As such it is unclear how homologous to the sequence of the referred to nucleic acid, a sequence must be to be included within the scope of these claims.

Claim 15 is drawn to the nucleic acid of claim 1, 2, 6-12, wherein the sequence comparison algorithm is FASTA version 3.9t78 with default parameters. There is no antecedent basis for the sequence comparison algorithm in claims 1 and 2.

Claim 16 is indefinite in that it is unclear to what sequence applicants intend the phrase "sequences substantially identical thereto" to refer. Is it applicants intent that sequences substantially identical thereto is referring to SEQ ID NO: 21, and thus the claimed nucleic acid must comprise 10 consecutive bases of SEQ ID NO: 21, sequences substantially identical thereto, and sequences complementary thereto. Or is it applicants intent that the claimed nucleic acid must comprise 10 consecutive bases of SEQ ID NO: 21, or sequences substantially identical thereto the 10 consecutive bases and sequences complementary thereto the 10 consecutive bases. In the interest of advancing prosecution, the claim has been interpreted as broadly as reasonable, such that the claimed nucleic acid must comprise 10 consecutive bases of SEQ ID NO: 21, or sequences substantially identical thereto the 10 consecutive bases and sequences complementary thereto the 10 consecutive bases.

Claims 17-21 are indefinite in that they are confusing in that they are drawn to a nucleic acid having at least 50% to 70% homology to the nucleic acid of claim 10, which

is drawn to a nucleic acid having at least 75% homology to the nucleic acid of claim 1, which is drawn to a nucleic acid having at least 50% identity to SEQ ID NO: 21. Is it applicants intent to claim the genus(s) of nucleic acids as described above?

Claims 6-14, 17-21 each recite a limitation of the claimed nucleic acid as having a % homology whereas claim 1 recites a limitation of the claimed nucleic acid as having a % identity. Claims 6-14 and 17-21 are indefinite in that it is unclear as to applicants intent in the use of homology versus identity in the claims. Similarly claims 67, 69-78, 82-85 refer to a % complementary. Depending on applicants intent it is suggested that applicants use consistency through out the application.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-5, 6-14, 15, 16-21, 22, 23, 40, 41, 67-81, 82-85 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3-5, 6-14, 15, 16, 17-21, 22, 23, are directed to all possible nucleic acids that hybridize to the nucleic acid of claim 1 under high to low stringency (claims 3-5), all possible nucleic acids having at least 55%, 60%, 65%, 70%, 75%, 80%, 5%, 90%, and 95% homology to the nucleic acid of claim 1 (claims 6-15, respectively), all possible

nucleic acids comprising at least 10 consecutive bases of the sequence of SEQ ID NO: 21 (claim 16), all possible nucleic acids having at least 55%, 60%, 65%, 70% and 75% homology to the nucleic acid of claim 10 (claims 17-21, respectively), all possible nucleic acids encoding a polypeptide having a sequence selected from SEQ ID NO 30, a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 30 , or sequences substantially identical thereto (claims 22and 23). Claims 40, 41 are directed to all possible methods of producing a any polypeptide having a sequence of SEQ ID NO: 30, a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 30 , or sequences substantially identical thereto, comprising recombinant expression of a nucleic acid encoding the polypeptide (claims 40 and 41). Claims 67-81, 82-85 are directed to all possible nucleic acid probes comprising an oligonucleotide of about 10 to 50 nucleotides in length and having an area of at least 10 contiguous nucleotides that is at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 5%, 90%, 95% and fully complementary to a nucleic acid target region of the nucleic acid sequence of SEQ ID NO: 21 and which hybridizes to the nucleic acid target region under moderate to highly stringent conditions to form a detectable target:probe duplex (claims 67-84). Claim 85 is directed to all possible polynucleotide probes having a sequence which is the same as or fully complementary to at least a portion of SEQ ID NO: 21.

The specification, however, only provides a single representative species, that nucleic acid having the sequence of SEQ ID NO: 21, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional

representative species of these nucleic acids by sufficient identifying structural characteristics or properties. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-5, 6-14, 15, 16, 17-21, 22, 23, 40, 41, 67-81, 82-85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide having phosphatase activity, wherein said polypeptide comprises SEQ ID NO: 30, does not reasonably provide enablement for any nucleic acid or polynucleotide probe which is fully complementary to a portion of SEQ ID NO: 21. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5, 6-14, 15, 16, 17-21, 22, 23, are so broad as to encompass any possible nucleic acid that hybridizes to the nucleic acid of claim 1 under high to low stringency (claims 1-5), any possible nucleic acid having at least 55%, 60%, 65%, 70%, 75%, 80%, 5%, 90%, and 95% homology to the nucleic acid of claim 1 (claims 6-15, respectively), any possible nucleic acid comprising at least 10 consecutive bases of the sequence of SEQ ID NO: 21 (claim 16), any possible nucleic acid having at least 55%, 60%, 65%, 70% and 75% homology to the nucleic acid of claim 10 (claims 17-21, respectively), any possible nucleic acid encoding a polypeptide having a sequence selected from SEQ ID NO 30, a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 30 , or sequences substantially identical thereto (claims 22and 23). Claims 40, 41 are so broad as to encompass any possible method of producing a polypeptide having a sequence of SEQ ID NO: 30, a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 30 , or sequences substantially identical thereto, comprising recombinant expression of a nucleic acid encoding the polypeptide (claims 40 and 41). Claims 67-81, 82-85 are so broad as to encompass any possible nucleic acid probe comprising an oligonucleotide of about 10 to 50 nucleotides in length and having an area of at least 10 contiguous nucleotides that is at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 5%, 90%, 95% and fully complementary to a nucleic acid target region of the nucleic acid sequence of SEQ ID NO: 21 and which hybridizes to the nucleic acid target region under moderate to highly stringent conditions to form a

detectable target:probe duplex (claims 67-84). Claim 85 is so broad as to encompass any possible polynucleotide probe having a sequence which is the same as or fully complementary to at least a portion of SEQ ID NO: 21.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acids broadly encompassed by the claims, including any nucleic acid or polynucleotide probe which is fully complementary to a portion of SEQ ID NO: 21. The claims rejected under this section of U.S.C. 112, first paragraph, insufficient structural and functional limits on the claimed nucleic acids. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence (and thus nucleic acid sequence) and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that isolated nucleic acid encoding a polypeptide having phosphatase activity, wherein said polypeptide comprises SEQ ID NO: 30.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any nucleic acid or polynucleotide probe which is fully complementary to at least a portion of SEQ ID NO: 21 or any nucleic acid which is substantially identical to SEQ ID NO: 2, because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without its functional activity; (B) the general tolerance of the claimed polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of the polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain functional/biological activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those nucleic acids of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of modifications of any nucleic acid encoding any phosphatase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 4, 5, 6-14, 15, 16, 17-21, 67-70, 79 and 85 are rejected under 35 U.S.C. 102(e) as being anticipated by Hirschberg et al. (U.S. Patent No: 5,792,903).

Hirschberg et al. teach a purified and isolated DNA sequence encoding lycopene cyclase. The cDNA taught by Hirschberg et al. is a 4928 base pair sequence of DNA with an open reading frame from 2029-3261 of SEQ ID NO: 1. Hirschberg et al. teach approximately 2000 bp of sequence upstream of the lycopene cyclase open reading

frame and included in this region is a region from nucleotide 1551 to 1565 (15 nucleotides) that is 86.67 % identical to SEQ ID NO: 21 from nucleotide 337 to 351, and thus Hirschberg et al. teach an isolated polynucleotide (probe) comprising an oligonucleotide from about 10 to 50 nucleotides in length and having an area of at least 10 contiguous nucleotides that is at least 50% complementary to a nucleic acid target region of the nucleic acid sequence selected from SEQ ID NO: 21, and which hybridizes under moderate to highly stringent conditions (See also above 112 second paragraph rejections).

Thus, claims 4, 5, 6-14, 15, 16, 17-21, 67-70, 79 and 85 are anticipated.

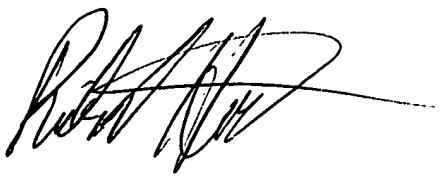
Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



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Art Unit 1652
March 21, 2003